

10/525006

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NEWS	9	APR 02	CAS Registry Number Crossover Limits Increased to 500,000 in Key STN Databases
NEWS	10	APR 02	PATDPAFULL: Application and priority number formats enhanced
NEWS	11	APR 02	DWPI: New display format ALLSTR available
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NEWS	13	APR 02	EMBASE Adds Unique Records from MEDLINE, Expanding Coverage back to 1948
NEWS	14	APR 07	CA/CAPLUS CLASS Display Streamlined with Removal of Pre-IPC 8 Data Fields
NEWS	15	APR 07	50,000 World Traditional Medicine (WTM) Patents Now Available in CAPLUS
NEWS	16	APR 07	MEDLINE Coverage Is Extended Back to 1947

NEWS EXPRESS FEBRUARY 15 10 CURRENT WINDOWS VERSION IS V8.4.2,
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=> FIL REGISTRY

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.22	0.22

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DICTIONARY FILE UPDATES: 13 JUN 2010 HIGHEST RN 1227570-00-4

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=> s 91714-92-2/rn

L1 0 91714-92-2/RN

=> s 91714-94-2/rn

L2 1 91714-94-2/RN

=> d 12

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2010 ACS on STN

RN **91714-94-2** REGISTRY

ED Entered STN: 16 Nov 1984

CN Benzeneacetic acid, 2-amino-3-(4-bromobenzoyl)- (CA INDEX NAME)

OTHER NAMES:

CN AHR 10282

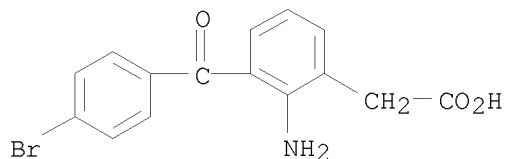
CN Bromfenac

CN Xibrom

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CN [2-Amino-3-(p-bromobenzoyl)phenyl]acetic acid
MF C15 H12 Br N O3
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CA, CAPLUS,
CHEMCATS, CIN, CSChem, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS,
IMSPRODUCT, IMSRESEARCH, IPA, MEDLINE, MRCK*, PROMT, PROUSDDR, PS,
RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

227 REFERENCES IN FILE CA (1907 TO DATE)
27 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
230 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s tyloxapol/cn

L3 1 TYLOXAPOL/CN

=> d 13

L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2010 ACS on STN
RN 25301-02-4 REGISTRY
ED Entered STN: 16 Nov 1984
CN Formaldehyde, polymer with oxirane and 4-(1,1,3,3-tetramethylbutyl)phenol
(CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Ethylene oxide, polymer with formaldehyde and
p-(1,1,3,3-tetramethylbutyl)phenol (8CI)
CN Oxirane, polymer with formaldehyde and 4-(1,1,3,3-tetramethylbutyl)phenol
(9CI)
CN Phenol, 4-(1,1,3,3-tetramethylbutyl)-, polymer with formaldehyde and
oxirane (9CI)
CN Phenol, p-(1,1,3,3-tetramethylbutyl)-, polymer with ethylene oxide and
formaldehyde (8CI)
OTHER NAMES:
CN Alevaire
CN Ethylene oxide-formaldehyde-4-(1,1,3,3-tetramethylbutyl)phenol copolymer
CN Ethylene oxide-formaldehyde-p-octylphenol copolymer
CN NSC 90255
CN Oxyethylated tertiary octyl-phenol-formaldehyde polymer
CN p-Isooctylpolyoxyethylenephenol formaldehyde polymer
CN Superinone
CN Triton A 20

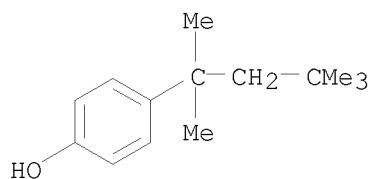
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CN Triton WR 1339
CN **Tyloxapol**
DR 9014-50-0, 9014-66-8, 9015-10-5
MF (C14 H22 O . C2 H4 O . C H2 O)x
CI PMS, COM
PCT Phenolic resin, Polyether, Polyether formed
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOSIS, BIOTECHNO,
CA, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU,
EMBASE, IPA, MEDLINE, MRCK*, PATDPASPC, PROMT, PS, RTECS*, TOXCENTER,
USAN, USPAT2, USPATFULL, USPATOLD, VETU
(*File contains numerically searchable property data)
Other Sources: DSL**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

CM 1

CRN 140-66-9
CMF C14 H22 O



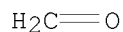
CM 2

CRN 75-21-8
CMF C2 H4 O



CM 3

CRN 50-00-0
CMF C H2 O



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

844 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

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844 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file medicine

FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	10.68	10.90

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FILE 'USPATOLD' ENTERED AT 16:01:31 ON 14 JUN 2010

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FILE 'USPAT2' ENTERED AT 16:01:31 ON 14 JUN 2010

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=> s l1 and l2

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L4 0 L1 AND L2

=> s bromfenac and tyloxapol

L5 150 BROMFENAC AND TYLOXAPOL

=> s ophthalmic

L6 263335 OPHTHALMIC

=> s l5 and l6

L7 111 L5 AND L6

=> dup rem

ENTER L# LIST OR (END):17

DUPLICATE IS NOT AVAILABLE IN 'ADISINSIGHT, ADISNEWS, DGENE, DRUGMONOG2, IMSPRODUCT, KOSMET, PCTGEN, USGENE'.

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PROCESSING COMPLETED FOR L7

L8 106 DUP REM L7 (5 DUPLICATES REMOVED)

=> s l8 and pd<2004

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'2004' NOT A VALID FIELD CODE
'2004' NOT A VALID FIELD CODE
15 FILES SEARCHED...
'2004' NOT A VALID FIELD CODE
22 FILES SEARCHED...
'2004' NOT A VALID FIELD CODE
27 FILES SEARCHED...
29 FILES SEARCHED...

L9 38 L8 AND PD<2004

=> s bromfenac sodium or bromfenac monosodium

L10 496 BROMFENAC SODIUM OR BROMFENAC MONOSODIUM

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=> s tyloxapol or alevaire or superinone or triton A 20 or triton WR 1339
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25 FILES SEARCHED...

30 FILES SEARCHED...

31 FILES SEARCHED...

L11 9953 TYLOXAPOL OR ALEVAIRE OR SUPERINONE OR TRITON A 20 OR TRITON WR
1339

=>

=> s l10 and l11

5 FILES SEARCHED...

L12 8 L10 AND L11

=> dup rem

ENTER L# LIST OR (END):l12

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PROCESSING COMPLETED FOR L12

L13 5 DUP REM L12 (3 DUPLICATES REMOVED)

=> d l13 1-5 ibib, kwic

L13 ANSWER 1 OF 5 USPATFULL on STN

ACCESSION NUMBER: 2008:362814 USPATFULL

TITLE: Transdermal Drug Delivery Formulation

INVENTOR(S): Singh, Jagat, Scarborough, CANADA

PATENT ASSIGNEE(S): NUVO RESEARCH INC., MISSISSAUGA, CANADA (non-U.S.
corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20080319092	A1	20081225
APPLICATION INFO.:	US 2006-3028	A1	20060804 (12)
	WO 2006-CA1271		20060804
			20080728 PCT 371 date

	NUMBER	DATE
PRIORITY INFORMATION:	US 2005-705498P	20050805 (60)
	US 2006-771030P	20060208 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	KATTEN MUCHIN ROSENMAN LLP, (C/O PATENT ADMINISTRATOR), 2900 K STREET NW, SUITE 200, WASHINGTON, DC, 20007-5118, US	
NUMBER OF CLAIMS:	2	

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EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Page(s)
LINE COUNT: 2115
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . Aminobenzoate Sodium; Anidoxime; Anileridine; Anileridine Hydrochloride; Anilopam Hydrochloride; Aniolac; Antipyrine; Aspirin; Benoxaprofen; Benzydamine Hydrochloride; Bicifadine Hydrochloride; Brifentanil Hydrochloride; Bromadoline Maleate; **Bromfenac Sodium**; Buprenorphine Hydrochloride; Butacetin; Butixirate; Butorphanol; Butorphanol Tartrate; Carbamazepine; Carbaspirin Calcium; Carbiphen Hydrochloride; Carfentanil Citrate; Ciprofadol Succinate; Ciramadol; Ciramadol Hydrochloride; Clonixeril; . . .
DETD . . . Trioxsalen; Triptorelin Pamoate; Trolamine Polypeptide Oleate Condensate; Trombodin; Trometamol; Tromethamine; Tropine Ester; Trospetomycin; Trovafloxacin; Trovafloxacin Mesylate; Troviridine; Tucareol; Tulobuterol; Tylogenin; **Tyloxapol**; Undecoyl Chloride; Undecoyl Chloride Iodine Complex; Unoprostone Isopropyl; Urapidil; Urea, C-13; Urea, C-14; Uridine Triphosphate; Valaciclovir; Valdecocix; Valganciclovir Hydrochloride; Valproate. . .

L13 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2010 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2007:1421955 CAPLUS
DOCUMENT NUMBER: 148:39746
TITLE: Bromfenac ophthalmic formulations and methods of use
INVENTOR(S): Sawa, Shirou; Fujita, Shuhei; Grillone, Lisa R.
PATENT ASSIGNEE(S): Ista Pharmaceuticals, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 21pp., Cont.-in-part of U.S. Ser. No. 525,006.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20070287749	A1	20071213	US 2007-755662	20070530
US 20050239895	A1	20051027	US 2005-525006	20050328
PRIORITY APPLN. INFO.:			JP 2003-12427	A 20030121
			US 2005-525006	A2 20050328
			WO 2004-JP350	W 20040116

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB . . . 2-amino-3-(4-bromobenzoyl)phenylacetic acid or its pharmacol. acceptable salt or a hydrate thereof, an alkyl aryl polyether alc. type polymer such as **tyloxapol**, or a polyethylene glycol fatty acid ester such as polyethylene glycol monostearate. The present invention further discloses new bromfenac ophthalmic. . .
IT 25301-02-4, **Tyloxapol** 25322-68-3D, Polyethylene glycol, esters
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bromfenac ophthalmic formulations and methods of use)
IT 91714-93-1, **Bromfenac sodium** 91714-94-2, Bromfenac
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

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(bromfenac ophthalmic formulations and methods of use)

L13 ANSWER 3 OF 5 USPATFULL on STN

ACCESSION NUMBER: 2007:308290 USPATFULL
TITLE: Penetration Enhancer Combinations for Transdermal
Delivery
INVENTOR(S): Mitragotri, Samir, Goleta, CA, UNITED STATES
Karande, Pankaj S., Somerville, MA, UNITED STATES
Jain, Amit K., Redwood City, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20070269379	A1	20071122
APPLICATION INFO.:	US 2004-560571	A1	20040721 (10)
	WO 2004-US23634		20040721
			20070202 PCT 371 date

	NUMBER	DATE
PRIORITY INFORMATION:	US 2003-560717P	20030723 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	Rober Berliner, Berliner & Associated, 555 W. Fifth Street, 31st Floor, Los Angeles, CA, 90013, US	
NUMBER OF CLAIMS:	52	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	18 Drawing Page(s)	
LINE COUNT:	4179	

DETD . . . Aminobenzoate Sodium; Amidoxime; Anileridine; Anileridine
Hydrochloride; Anilopam Hydrochloride; Aniolac; Antipyrine; Aspirin;
Benoxaprofen; Benzydamine Hydrochloride; Bicifadine Hydrochloride;
Brifentanil Hydrochloride; Bromadoline Maleate; **Bromfenac**
Sodium; Buprenorphine Hydrochloride; Butacetin; Butixirate;
Butorphanol; Butorphanol Tartrate; Carbamazepine; Carbaspirin Calcium;
Carbiphen Hydrochloride; Carfentanil Citrate; Ciprofadol Succinate;
Ciramadol; Ciramadol Hydrochloride; Clonixeril; . . .
DETD . . . Trioxsalen; Triptorelin Pamoate; Trolamine Polypeptide Oleate
Condensate; Trombodipine; Trometarnol; Tromethamine; Tropine Ester;
Trospectomycin; Trovafloxacin; Trovafloxacin Mesylate; Trovirdine;
Tucaresol; Tulobuterol; Tylogenin; **Tyloxapol**; Undecoylium
Chloride; Undecoylium Chloride Iodine Complex; Unoprostone Isopropyl;
Urapidil; Urea, C-13; Urea, C-14; Uridine Triphosphate; Valaciclovir;
Valdecocix; Valganciclovir Hydrochloride; Valproate. . .

L13 ANSWER 4 OF 5 USPATFULL on STN

ACCESSION NUMBER: 2007:95155 USPATFULL
TITLE: Aqueous solution preparation containing aminoglycoside
antibiotic and bromfenac
INVENTOR(S): Sawa, Shirou, 366-1-105, MINAMIBEFU 4-CHOME, NISHI-KU,
KOBE-SHI, HYOGO, JAPAN 651-2116

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20070082857	A1	20070412

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APPLICATION INFO.: US 2004-578359 A1 20041112 (10)
 WO 2004-JP16849 20041112
 20060606 PCT 371 date

	NUMBER	DATE
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PRIORITY INFORMATION:	JP 2003-384646	20031114
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	WENDEROTH, LIND & PONACK, L.L.P., 2033 K STREET N. W., SUITE 800, WASHINGTON, DC, 20006-1021, US	
NUMBER OF CLAIMS:	8	
EXEMPLARY CLAIM:	1	
LINE COUNT:	807	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM The nonionic surfactant includes, for example, polyoxyethylene sorbitan fatty acid esters (e.g. polysorbate 20, polysorbate 60, polysorbate 80, etc.); tyloxapol; polyoxyl 40 monostearate; polyoxyethylene hydrogenated castor oil (e.g. polyoxyethylene (40) hydrogenated castor oil, polyoxyethylene (60) hydrogenated castor oil, etc.); poloxamer; and the like. Preferable examples of the nonionic surfactant are polysorbate 80, tyloxapol or polyoxyl 40 monostearate.

SUMM . . . polymer (e.g. povidone K-30, polyvinyl alcohol, α -cyclodextrin, etc.); citric acid or its pharmacologically acceptable salt and a nonionic surfactant (e.g. tyloxapol, polysorbate 80, polyoxyl 40 monostearate, etc.); monoethanolamine or its pharmacologically acceptable salt and a nonionic water-soluble polymer (e.g. povidone K-30, polyvinyl alcohol, α -cyclodextrin, etc.); monoethanolamine or its pharmacologically acceptable salt and a nonionic surfactant (e.g. tyloxapol, polysorbate 80, polyoxyl 40 monostearate, etc.); N-methylglucamine or its pharmacologically acceptable salt and a nonionic water-soluble polymer (e.g. povidone K-30, polyvinyl alcohol, α -cyclodextrin, etc.); N-methylglucamine or its pharmacologically acceptable salt and a nonionic surfactant (e.g. tyloxapol, polysorbate 80; polyoxyl 40 monostearate, etc.); nicotinamide and a nonionic water-soluble polymer (e.g. povidone K-30, polyvinyl alcohol, α -cyclodextrin, etc.); nicotinamide and a nonionic surfactant (e.g. tyloxapol, polysorbate 80, polyoxyl 40 monostearate, etc.); a nonionic surfactant (e.g. tyloxapol, polysorbate 80, polyoxyl 40 monostearate, etc.) and a nonionic water-soluble polymer (e.g. povidone K-30, polyvinyl alcohol, α -cyclodextrin, etc.), or the . . .

SUMM . . . purified water or water for injections), and to this solution were added an aminoglycoside antibiotic (e.g. gentamicin sulfate, etc.) and bromfenac sodium. The mixture was dissolved and adjusted to a pH of about not less than 7.0, preferably to a pH of. . .

SUMM . . . solvent, thereby to prepare a solution. To the solution were added an aminoglycoside antibiotic (e.g. tobramycin, gentamicin sulfate, etc.) and bromfenac sodium, and the resulting solution was adjusted to a pH of about not less than 7.0, preferably 7.5 to 8.5.

SUMM . . . above, thereby to prepare a solution. To the solution were added an aminoglycoside antibiotic (e.g. tobramycin, gentamicin sulfate,

etc.) and **bromfenac sodium**, and the resulting solution was adjusted to a pH of about not less than 6.0, preferably 7.5 to 8.5.

SUMM . . . example, blepharitis, hordeolum, conjunctivitis, keratitis, dacryocystitis, etc. The dose in the case where an eye drop comprising 0.1 w/v % **bromfenac sodium** hydrate and 0.3 w/v % tobramycin or 0.3 w/v % gentamicin sulfate is applied may be 1 to 2 drops. . . .

SUMM In the case where the aqueous solution preparation of the present invention comprising, for example, 0.1 w/v % **bromfenac sodium** hydrate and 0.3 w/v % tobramycin or 0.3 w/v % gentamicin sulfate is applied in the form of a nose. . . .

SUMM In the case where the aqueous solution preparation of the present invention comprising, for example, 0.1 w/v % **bromfenac sodium** hydrate and 0.3 w/v % tobramycin or 0.3 w/v % gentamicin sulfate is applied in the form of an ear. . . .

SUMM . . . various infectious diseases by the aqueous solution preparation of the present invention, an injection comprising, for example, 0.1 w/v % **bromfenac sodium** hydrate and 0.3 w/v % tobramycin or 0.3 w/v % gentamicin sulfate may be applied intramuscularly or subcutaneously in an. . . .

DETD . . . 1 was prepared by dissolving boric acid and borax in a fixed amount of purified water and adding tobramycin and **bromfenac sodium** to the solution, followed by dissolution. With respect to the formulation 2, sodium citrate was further added to the formulation. . . . was prepared by dissolving boric acid and borax in a fixed amount of purified water and adding gentamicin sulfate and **bromfenac sodium** thereto to make a solution. Then, the pH values of these formulations were adjusted by addition of hydrochloric acid and. . . .

DETD A combination solution comprising tobramycin and **bromfenac sodium** as shown in Table 3 was prepared (formulation 4). Boric acid and borax were added to and dissolved in a fixed amount of purified water, and to this solution were added tobramycin and **bromfenac sodium**, followed by dissolution. Separately, each additive was added to and dissolved in the prescribed amount of purified water to give. . . . determined according to the criteria as described in Example 1.

TABLE 3

Formulation of combination solution

		Formulation 4
Component		w/v %
<u>Bromfenac sodium</u>		0.2
Tobramycin		0.6
Boric acid		1.14
Borax		4.5
Hydrochloric acid		q.s.
Sodium hydroxide		q.s.
Purified water		q.s.
DETD	. . . sorbate	0.4
	Sodium glutamate	0.6
	N-Methyl-2-pyrrolidone	2.0

	Povidone K-30	4.0	
	Sodium alginate	0.2	
	Sodium chondroitin sulfate	2.0	
	Polysorbate 80	0.6	
	<u>Tyloxapol</u>	0.6	
	Polyoxyl 40 monostearate	0.6	
	Benzalkonium chloride	0.2	
	Sodium lauryl sulfate	0.2	
DETD	. . . alginate	0.1 w/v %	strongly
			turbid
	Sodium chondroitin sulfate	1.0 w/v %	strongly
			turbid
	Polysorbate 80	0.3 w/v %	clear
	<u>Tyloxapol</u>	0.3 w/v %	clear
	Polyoxyl 40 monostearate	0.3 w/v %	clear
	Benzalkonium chloride	0.1 w/v %	strongly
			turbid
	Sodium lauryl. . .		
DETD	. . . monoethanolamine and N-methylglucamine; nicotinamide; a nonionic water-soluble polymer such as povidone K-30; or a nonionic surfactant such as polysorbate 80, <u>tyloxapol</u> , and polyoxyl 40 monostearate.		
DETD	Combination solutions comprising gentamicin sulfate and <u>bromfenac sodium</u> as shown in Table 6 were prepared (formulations 5 and 6). The formulation 5 was prepared by adding sodium dihydrogen phosphate and concentrated glycerine to a fixed amount of purified water, dissolving the mixture, and adding gentamicin sulfate and <u>bromfenac sodium</u> thereto, followed by dissolution. With respect to the formulation 6, boric acid and borax was added to and dissolved in a fixed amount of purified water, and to this solution were added gentamicin sulfate and <u>bromfenac sodium</u> , and then the mixture was dissolved. Separately, each additive solution was prepared as shown in Table 7. Each additive was.		
	. . . to the criteria as described in Example 1.		

TABLE 6

Component	Formulation of combination solution (w/v %)	
	Formulation 5	Formulation 6
<u>Bromfenac sodium</u>	0.2	0.2
Gentamicin sulfate	0.6	0.6
Boric acid	--	1.14
Borax	--	4.5
Sodium dihydrogen phosphate	0.2	--
Concentrated glycerine	5.2	--
Hydrochloric acid	q.s.	q.s.
Sodium. . .		
DETD	. . . 2.0	
	Nicotinamide	2.0
	Potassium sorbate	0.4
	Povidone K-30	4.0
	Polyvinyl alcohol	2.0

	α -Cyclodextrin	4.0			
	Sodium alginate	0.2			
	Polysorbate 80	0.6			
	<u>Tyloxapol</u>	0.6			
	Polyoxyl 40 monostearate	0.6			
	Benzalkonium chloride	0.2			
	Sodium lauryl sulfate	0.2			
DETD	. . .	6.0	Clear		
Sodium alginate	0.1	Formulation 6	6.5	Strongly turbid	
Polysorbate 80	0.3	Formulation 6	6.5	Clear	
Polysorbate 80	0.3	Formulation 6	6.0	Clear	
<u>Tyloxapol</u>	0.3	Formulation 6	6.5	Clear	
Polyoxyl 40 monostearate	0.3	Formulation 6	6.5	Clear	
Benzalkonium chloride	0.1	Formulation 6	6.5	Strongly turbid	
Sodium lauryl	0.1	Formulation.	. . .		
DETD	. . .	nicotinamide; a nonionic water-soluble polymer such as povidone, polyvinyl alcohol, and α -cyclodextrin; or a nonionic surfactant such as polysorbate 80, <u>tyloxapol</u> , and polyoxyl 40 monostearate. Furthermore, when α -cyclodextrin as a nonionic water-soluble polymer, or polysorbate 80 as a nonionic surfactant was.			
	. . .				
DETD					
TABLE 9					

	<u>Bromfenac sodium</u> 3/2 hydrate	0.1	g
	Tobramycin	0.3	g
	Boric acid	1.4	g
	Borax	0.8	g
	Hydrochloric acid	q.s.	
	Purified water	q.s.	
. . .			
DETD	Borax was dissolved in about 80 ml of purified water. Tobramycin and <u>bromfenac sodium</u> were added to the solution, and the mixture was dissolved. To the solution was added boric acid, and the mixture. . .		
DETD			
TABLE 10			

	<u>Bromfenac sodium</u> 3/2 hydrate	0.1	g
	Tobramycin	0.3	g
	Boric acid	1.8	g
	Sodium citrate	0.3	g
	Sodium hydroxide	q.s.	
	Purified water. . .		
DETD	Tobramycin and <u>bromfenac sodium</u> were added to and dissolved in about 80 ml of purified water. To the solution were added sodium citrate and. . .		
DETD			
TABLE 11			

<u>Bromfenac sodium</u> 3/2 hydrate	0.1	g
Gentamicin sulfate	0.3	g
Polysorbate 80	0.3	g
Sodium dihydrogen phosphate	0.1	g
Concentrated glycerine	2.6. . .	

DETD . . . were added to and dissolved in about 80 ml of purified water. To the solution were added gentamicin sulfate and **bromfenac sodium**, and the mixture was dissolved. Sodium hydroxide was added to the solution to adjust the pH, and purified water was. . .

DETD

TABLE 12

<u>Bromfenac sodium</u> 3/2 hydrate	0.1	g
Tobramycin	0.3	g
Boric acid	1.6	g
Povidone K-30	2.0	g
Sodium hydroxide	q.s.	
Purified water. . .		

DETD Tobramycin and **bromfenac sodium** were added to and dissolved in about 80 ml of purified water. To the solution were added povidone K-30 and. . .

DETD

TABLE 13

<u>Bromfenac sodium</u> 3/2 hydrate	0.1	g
Tobramycin	0.3	g
Boric acid	1.6	g
N-Methylglucamine	1.0	g
Sodium hydroxide	q.s.	
Purified water	q.s.	

. . .
DETD Tobramycin and **bromfenac sodium** were added to and dissolved in about 80 ml of purified water. To the solution were added N-methylglucamine and boric. . .

DETD

TABLE 14

<u>Bromfenac sodium</u> 3/2 hydrate	0.1	g
Tobramycin	0.3	g
Boric acid	1.6	g
Borax	0.6	g
Povidone K-30	1.0	g
N-Methylglucamine	0.1. . .	

DETD Tobramycin and **bromfenac sodium** were added to and dissolved in about 80 ml of purified water. To the solution were added povidone K-30, N-methylglucamine,. . .

DETD

TABLE 15

<u>Bromfenac sodium</u> 3/2 hydrate	0.1	g
Tobramycin	0.3	g
Boric acid	1.6	g
Borax	0.7	g
Benzalkonium chloride	0.005	g
<u>Tyloxapol</u>	0.02	g
Povidone K-30	1.0	g
Sodium edetate	0.02	g
Sodium hydroxide	q.s.	
Purified water	q.s.	
Total volume	100	ml

DETD . . . Tobramycin and **bromfenac sodium** were added to and dissolved in about 80 ml of purified water. To the solution were added **tyloxapol**, povidone K-30, sodium edetate, benzalkonium chloride, boric acid and borax, and the mixture was dissolved. The pH of the solution. . .

DETD . . . it is possible to obtain a clear aqueous solution preparation comprising an aminoglycoside antibiotic or its pharmacologically acceptable salt and **bromfenac sodium** or its pharmacologically acceptable salt.

IT 68-04-2, Sodium citrate 77-92-9, Citric acid, biological studies
 98-92-0, Nicotinic acid amide 141-43-5, Monoethanolamine, biological studies
 1403-66-3, Gentamicin 1405-41-0, Gentamicin sulfate
 6284-40-8, N-Methylglucamine 32986-56-4, Tobramycin 91714-93-1,
Bromfenac sodium 91714-94-2
 (aqueous solns. containing aminoglycoside antibiotic and bromfenac)

L13 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2010 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2006:439980 CAPLUS

DOCUMENT NUMBER: 144:440131

TITLE: Aqueous eye drops with accelerated intraocular migration

INVENTOR(S): Sawa, Shirou; Fujimoto, Tomoko

PATENT ASSIGNEE(S): Senju Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
WO 2006049250	A1	20060511	WO 2005-JP20302	20051104
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,				

10/525006

IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM
CA 2560559 A1 20060511 CA 2005-2560559 20051104
CN 1993118 A 20070704 CN 2005-80025963 20051104
EP 1808170 A1 20070718 EP 2005-805529 20051104
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR
US 20070021507 A1 20070125 US 2006-568418 20060426
IN 2006KN02763 A 20070601 IN 2006-KN2763 20060921
MX 2007001172 A 20070312 MX 2007-1172 20070129
PRIORITY APPLN. INFO.: JP 2004-322569 A 20041105
WO 2005-JP20302 W 20051104

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB . . . inflammatory diseases on the external segment or anterior segment
of the eye. For example, an aqueous eye drop solution contained
bromfenac sodium hydrate 0.1, aminoethylsulfonic acid
0.5, benzalkonium chloride 0.005, tyloxapol 0.02, povidone 2,
sodium edetate 0.02, boric acid 1.3, borax 0.74, NaOH q.s., and distilled
water balance to 100 %.

=> d his

(FILE 'HOME' ENTERED AT 15:59:56 ON 14 JUN 2010)

FILE 'REGISTRY' ENTERED AT 16:00:17 ON 14 JUN 2010

L1 0 S 91714-92-2/RN
L2 1 S 91714-94-2/RN
L3 1 S TYLOXAPOL/CN

FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CAPLUS, DDFB,
DGENE, DISSABS, DRUGB, DRUGMONOG2, DRUGU, EMBAL, EMBASE, ESBIODASE,
IFIPAT, IMSDRUGNEWS, IMSPRODUCT, IPA, KOSMET, LIFESCI, MEDLINE,
NAPRALERT, NLDB, PASCAL, PCTGEN, SCISEARCH, TOXCENTER, ...' ENTERED AT
16:01:31 ON 14 JUN 2010

L4 0 S L1 AND L2
L5 150 S BROMFENAC AND TYLOXAPOL
L6 263335 S OPHTHALMIC
L7 111 S L5 AND L6
L8 106 DUP REM L7 (5 DUPLICATES REMOVED)
L9 38 S L8 AND PD<2004
L10 496 S BROMFENAC SODIUM OR BROMFENAC MONOSODIUM
L11 9953 S TYLOXAPOL OR ALEVAIRE OR SUPERINONE OR TRITON A 20 OR TRITON
L12 8 S L10 AND L11
L13 5 DUP REM L12 (3 DUPLICATES REMOVED)

=> d 19 30-38 ibib, kwic

L9 ANSWER 30 OF 38 USPATFULL on STN
ACCESSION NUMBER: 1999:160081 USPATFULL

Jagoe

10/525006

TITLE: Esters of non-steroidal anti-inflammatory carboxylic acids
INVENTOR(S): Hellberg, Mark, Arlington, TX, United States
Delgado, Pete, Fort Worth, TX, United States
Nixon, Jon C., Mansfield, TX, United States
PATENT ASSIGNEE(S): Alcon Laboratories, Inc., Fort Worth, TX, United States
(U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5998465		19991207 <--
APPLICATION INFO.:	US 1998-139506		19980825 (9)
RELATED APPLN. INFO.:	Division of Ser. No. US 1998-23385, filed on 13 Feb 1998 which is a division of Ser. No. US 1995-526913, filed on 12 Sep 1995, now patented, Pat. No. US 5750564		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Mach, D. Margaret		
LEGAL REPRESENTATIVE:	Mayo, Michael C.		
NUMBER OF CLAIMS:	30		
EXEMPLARY CLAIM:	1		
LINE COUNT:	786		
CAS INDEXING IS AVAILABLE FOR THIS PATENT.			

SUMM . . . using the compounds and compositions of the present invention to prevent and treat inflammatory disorders including ocular inflammation associated with ophthalmic disease and ophthalmic surgery.

SUMM . . . acid
indoprofen
pirprofen clidanac fenoprofen
naproxen fenclorac meclofenamate
benoxaprofen carprofen isofezolac
aceloferac fenbufen etodolic acid
fleclozic acid amfenac efenamic acid
bromfenac ketoprofen fencloenac
alcofenac orpanoxin zomopirac
diflunisal pranoprofen zaltoprofen

DETD The present invention is particularly directed to the provision of compositions adapted for treatment of ophthalmic tissues. The ophthalmic compositions of the present invention will include one or more compounds of formulas (I) and (II) and a pharmaceutically acceptable. . . semi-solid compositions. Suspensions may be preferred for compounds of formulas (I) and (II) which are relatively insoluble in water. The ophthalmic compositions of the present invention may also include various other ingredients, such as buffers, preservatives, co-solvents and viscosity building agents.

DETD Ophthalmic products are typically packaged in multidose form. Preservatives are thus required to prevent microbial contamination during use. Suitable preservatives include: . . .

DETD . . . the formulations, to decrease physical separation of components of a suspension or emulsion of formulation and/or otherwise to improve the ophthalmic formulation. Such viscosity building agents

include, for example, polyvinyl alcohol, polyvinyl pyrrolidone, methyl cellulose, hydroxypropyl methylcellulose, hydroxyethyl cellulose, carboxymethyl cellulose, . . .

DETD As indicated above, use of the compounds of formulas (I) and (II) to prevent or reduce damage to ophthalmic tissues at the cellular level is a particularly important aspect of the present invention. Ophthalmic conditions which may be treated include, but are not limited to, cataracts, retinopathies, hereditary degenerative diseases, macular degeneration, ocular ischemia, glaucoma, and damage associated with injuries to ophthalmic tissues, such as ischemia reperfusion injuries, photochemical injuries, and injuries associated with ocular surgery, particularly injuries to the retina, cornea. . . . other tissues caused by exposure to light or surgical instruments. The compounds may also be used as an adjunct to ophthalmic surgery, such as by vitreal or subconjunctival injection following ophthalmic surgery. The compounds may be used for acute treatment of temporary conditions, or may be administered chronically, especially in the case of degenerative disease. The compounds may also be used prophylactically, especially prior to ocular surgery or noninvasive ophthalmic procedures, or other types of surgery.

DETD Topical ophthalmic compositions useful for treating inflammation and/or tissue oxidative damage:

DETD

Component	% w/v
-----------	-------

Compound	0.05-5.0
----------	----------

Tyloxapol 0.01-0.05

HPMC 0.5

Benzalkonium Chloride 0.01

Sodium Chloride 0.8

Edetate Disodium 0.01

NaOH/HCl q.s. pH 7.4

Purified Water q.s. 100. . . .

DETD A preferred topical ophthalmic composition useful for treating inflammation and/or tissue oxidative damage:

DETD

Component	% w/v
-----------	-------

Compound E	0.10
------------	------

Tyloxapol 0.01-0.05

HPMC 0.5

Benzalkonium Chloride 0.01

Sodium Chloride 0.8

Edetate Disodium 0.01

NaOH/HCl q.s. pH 7.4

Purified Water q.s. 100. . . .

DETD . . . either dry heat or filtered. The sterilized anti-inflammatory agent is weighed aseptically and placed into a pressurized ballmill container. The tyloxapol, in sterilized aqueous solution form, is then added to the ballmill container. Sterilized glass balls are then added to the. . . .

CLM What is claimed is:

. . . acid; indoprofen; piroprofen; clidanac; fenoprofen; naproxen; fenclorac; meclofenamate; benoxaprofen; carprofen; isofezolac;

aceloferac; fenbufen; etodolic acid; fleclozic acid; amfenac; efenamic acid; **bromfenac**; ketoprofen; fenclofenac; alcofenac; orpanoxin; zomopirac; diflunisal; flufenamic acid; niflumic acid; mefenamic acid; pranoprofen; zaltoprofen; indomethacin; sulindac; tolmetin; suprofen; ketorolac; flurbiprofen;. . .

CLM What is claimed is:

. . . acid; indoprofen; pirprofen; clidanac; fenoprofen; naproxen; fenclofac; meclofenamate; benoxaprofen; carprofen; isofezolac; aceloferac; fenbufen; etodolic acid; fleclozic acid; amfenac; efenamic acid; **bromfenac**; ketoprofen; fenclofenac; alcofenac; orpanoxin; zomopirac; diflunisal; flufenamic acid; niflumic acid; mefenamic acid; pranoprofen; zaltoprofen; indomethacin; sulindac; tolmetin; suprofen; ketorolac; flurbiprofen;. . .

CLM What is claimed is:

24. The method according to claim 23, wherein the composition is administered to prevent or alleviate damage to ophthalmic tissues.

CLM What is claimed is:

. . . acid; indoprofen; pirprofen; clidanac; fenoprofen; naproxen; fenclofac; meclofenamate; benoxaprofen; carprofen; isofezolac; aceloferac; fenbufen; etodolic acid; fleclozic acid; amfenac; efenamic acid; **bromfenac**; ketoprofen; fenclofenac; alcofenac; orpanoxin; zomopirac; diflunisal; flufenamic acid; niflumic acid; mefenamic acid; pranoprofen; zaltoprofen; indomethacin; sulindac; tolmetin; suprofen; ketorolac; flurbiprofen;. . .

IT Drug delivery systems

(ophthalmic; preparation of esters of non-steroidal antiinflammatory agents with antioxidant activity)

L9 ANSWER 31 OF 38 USPATFULL on STN

ACCESSION NUMBER: 1999:63322 USPATFULL

TITLE: Anti-oxidant esters of non-steroidal anti-inflammatory agents

INVENTOR(S): Hellberg, Mark, Arlington, TX, United States
Delgado, Pete, Fort Worth, TX, United States
Nixon, Jon C., Mansfield, TX, United States

PATENT ASSIGNEE(S): Alcon Laboratories, Inc., Fort Worth, TX, United States
(U.S. corporation)

	NUMBER	KIND	DATE	
	-----	-----	-----	
PATENT INFORMATION:	US 5908849		19990601	<--
APPLICATION INFO.:	US 1998-23385		19980213	(9)
RELATED APPLN. INFO.:	Division of Ser. No. US 1995-526913, filed on 12 Sep 1995, now patented, Pat. No. US 5750564			
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Rotman, Alan L.			
ASSISTANT EXAMINER:	Mach, Margaret M.			
LEGAL REPRESENTATIVE:	Mayo, Michael C.			
NUMBER OF CLAIMS:	30			
EXEMPLARY CLAIM:	1			
LINE COUNT:	797			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . using the compounds and compositions of the present invention to prevent and treat inflammatory disorders including ocular inflammation associated with ophthalmic disease and ophthalmic surgery.

SUMM

loxoprofen	tolfenamic acid	
		indoprofen
pirprofen	clidanac	fenoprofen
naproxen	fenclorac	meclofenamate
benoxaprofen	carprofen	isofezolac
aceloferac	fenbufen	etodolic acid
fleclozic acid		
	amfenac	efenamic acid
<u>bromfenac</u>	ketoprofen	fenclofenac
alcofenac	orpanoxin	zomopirac
diflunisal	pranoprofen	zaltoprofen

DETD The present invention is particularly directed to the provision of compositions adapted for treatment of ophthalmic tissues. The ophthalmic compositions of the present invention will include one or more compounds of formulas (I) and (II) and a pharmaceutically acceptable. . . semi-solid compositions. Suspensions may be preferred for compounds of formulas (I) and (II) which are relatively insoluble in water. The ophthalmic compositions of the present invention may also include various other ingredients, such as buffers, preservatives, co-solvents and viscosity building agents.

DETD Ophthalmic products are typically packaged in multidose form. Preservatives are thus required to prevent microbial contamination during use. Suitable preservatives include: . . .

DETD . . . the formulations, to decrease physical separation of components of a suspension or emulsion of formulation and/or otherwise to improve the ophthalmic formulation. Such viscosity building agents include, for example, polyvinyl alcohol, polyvinyl pyrrolidone, methyl cellulose, hydroxypropyl methylcellulose, hydroxyethyl cellulose, carboxymethyl cellulose, . . .

DETD As indicated above, use of the compounds of formulas (I) and (II) to prevent or reduce damage to ophthalmic tissues at the cellular level is a particularly important aspect of the present invention. Ophthalmic conditions which may be treated include, but are not limited to, cataracts, retinopathies, hereditary degenerative diseases, macular degeneration, ocular ischemia, glaucoma, and damage associated with injuries to ophthalmic tissues, such as ischemia reperfusion injuries, photochemical injuries, and injuries associated with ocular surgery, particularly injuries to the retina, cornea. . . other tissues caused by exposure to light or surgical instruments. The compounds may also be used as an adjunct to ophthalmic surgery, such as by vitreal or subconjunctival injection following ophthalmic surgery. The compounds may be used for acute treatment of temporary conditions, or may be administered chronically, especially in the case of degenerative disease. The compounds may also be used prophylactically, especially prior to ocular surgery or noninvasive ophthalmic procedures, or other types of surgery.

DETD Topical ophthalmic compositions useful for treating inflammation and/or tissue oxidative damage:

DETD

Component	% w/v
Compound	0.05-5.0
<u>Tyloxapol</u>	0.01-0.05
HPMC	0.5
Benzalkonium Chloride	0.01
Sodium Chloride	0.8
Edetate Disodium	0.01
NaOH/HCl	q.s. pH 7.4
Purified Water	q.s. 100 mL

DETD A preferred topical ophthalmic composition useful for treating inflammation and/or tissue oxidative damage:

DETD

Component	% w/v
Compound E	0.10
<u>Tyloxapol</u>	0.01-0.05
HPMC	0.5
Benzalkonium Chloride	0.01
Sodium Chloride	0.8
Edetate Disodium	0.01
NaOH/HCl	q.s. pH 7.4
Purified Water	q.s. 100 mL

DETD . . . either dry heat or filtered. The sterilized anti-inflammatory agent is weighed aseptically and placed into a pressurized ballmill container. The tyloxapol, in sterilized aqueous solution form, is then added to the ballmill container. Sterilized glass balls are then added to the. . .

CLM What is claimed is:

. . . acid; indoprofen; piroprofen; clidanac; fenoprofen; naproxen; fenclozic; meclofenamate; benoxaprofen; carprofen; isofezolac; acetoferac; fenbuten; etodolic acid; fenclozic acid; amfenac; efenamic acid; **bromfenac**; ketoprofen; fenclofenac; alcofenac; orpanoxin; zomopirac; diflunisal; flufenamic acid; niflumic acid; mefenamic acid; pranoprofen; zaltoprofen; indomethacin; sulindac; tolmetin; suprofen; ketorolac; flurbiprofen;. . .

CLM What is claimed is:

. . . acid; indoprofen; piroprofen; clidanac; fenoprofen; naproxen; fenclozic; meclofenamate; benoxaprofen; carprofen; isofezolac; acetoferac; fenbuten; etodolic acid; fenclozic acid; amfenac; efenamic acid; **bromfenac**; ketoprofen; fenclofenac; alcofenac; orpanoxin; zomopirac; diflunisal; flufenamic acid; niflumic acid; mefenamic acid; pranoprofen; zaltoprofen; indomethacin; sulindac; tolmetin; suprofen; ketorolac; flurbiprofen;. . .

CLM What is claimed is:

24. The method according to claim 23, wherein the composition is administered to prevent or alleviate damage to ophthalmic tissues.

10/525006

CLM What is claimed is:

. . . acid; indoprofen; pirprofen; clidanac; fenoprofen; naproxen;
fenclorac; meclofenamate; benoxaprofen; carprofen; isofezolac;
aceloferac; fenbufen; etodolic acid; fleclozic acid; amfenac; efenamic
acid; **bromfenac**; ketoprofen; fenclofenac; alcofenac;
orpanoxin; zomopirac; diflunisal; flufenamic acid; niflumic acid;
mefenamic acid; pranoprofen; zaltoprofen; indomethacin; sulindac;
tolmetin; suprofen; ketorolac; flurbiprofen;. . .

IT Drug delivery systems

(**ophthalmic**; preparation of esters of non-steroidal
antiinflammatory agents with antioxidant activity)

L9 ANSWER 32 OF 38 USPATFULL on STN

ACCESSION NUMBER: 1998:51640 USPATFULL

TITLE: Anti-oxidant esters of non-steroidal anti-inflammatory
agents

INVENTOR(S): Hellberg, Mark, 52211 Overridge Dr., Arlington, TX,
United States 76017
Delgado, Pete, 4315 N. Segura Ct., Fort Worth, TX,
United States 76132
Nixon, Jon C., 1616 Hastings Dr., Mansfield, TX, United
States 76132

	NUMBER	KIND	DATE	
	-----	-----	-----	
PATENT INFORMATION:	US 5750564		19980512	<--
APPLICATION INFO.:	US 1995-526913		19950912	(8)
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Richter, Johann			
ASSISTANT EXAMINER:	Stockton, Laura L.			
LEGAL REPRESENTATIVE:	Mayo, Michael C.			
NUMBER OF CLAIMS:	30			
EXEMPLARY CLAIM:	1			
LINE COUNT:	744			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . using the compounds and compositions of the present invention
to prevent and treat inflammatory disorders including ocular
inflammation associated with **ophthalmic** disease and
ophthalmic surgery.

SUMM

loxoprofen	tolfenamic acid	
		indoprofen
pirprofen	clidanac	fenoprofen
naproxen	fenclorac	meclofenamate
benoxaprofen	carprofen	isofezolac
aceloferac	fenbufen	etodolic acid
fleclozic acid		
	amfenac	efenamic acid
bromfenac	ketoprofen	fenclofenac
alcofenac	orpanoxin	zomopirac
diflunisal	pranoprofen	zaltoprofen

Jagoe

- DETD The present invention is particularly directed to the provision of compositions adapted for treatment of ophthalmic tissues. The ophthalmic compositions of the present invention will include one or more compounds of formulas (I) and (II) and a pharmaceutically acceptable. . . . semi-solid compositions. Suspensions may be preferred for compounds of formulas (I) and (II) which are relatively insoluble in water. The ophthalmic compositions of the present invention may also include various other ingredients, such as buffers, preservatives, co-solvents and viscosity building agents.
- DETD Ophthalmic products are typically packaged in multidose form. Preservatives are thus required to prevent microbial contamination during use. Suitable preservatives include:. . . .
- DETD . . . the formulations, to decrease physical separation of components of a suspension or emulsion of formulation and/or otherwise to improve the ophthalmic formulation. Such viscosity building agents include, for example, polyvinyl alcohol, polyvinyl pyrrolidone, methyl cellulose, hydroxypropyl methylcellulose, hydroxyethyl cellulose, carboxymethyl cellulose,. . . .
- DETD As indicated above, use of the compounds of formulas (I) and (II) to prevent or reduce damage to ophthalmic tissues at the cellular level is a particularly important aspect of the present invention. Ophthalmic conditions which may be treated include, but are not limited to, cataracts, retinopathies, hereditary degenerative diseases, macular degeneration, ocular ischemia, glaucoma, and damage associated with injuries to ophthalmic tissues, such as ischemia reperfusion injuries, photochemical injuries, and injuries associated with ocular surgery, particularly injuries to the retina, cornea. . . . other tissues caused by exposure to light or surgical instruments. The compounds may also be used as an adjunct to ophthalmic surgery, such as by vitreal or subconjunctival injection following ophthalmic surgery. The compounds may be used for acute treatment of temporary conditions, or may be administered chronically, especially in the case of degenerative disease. The compounds may also be used prophylactically, especially prior to ocular surgery or noninvasive ophthalmic procedures, or other types of surgery.
- DETD Topical ophthalmic compositions useful for treating inflammation and/or tissue oxidative damage:

DETD

Component	% w/v
Compound	0.05-5.0
<u>Tyloxapol</u>	0.01-0.05
HPMC	0.5
Benzalkonium Chloride	0.01
Sodium Chloride	0.8
Edetate Disodium	0.01
NaOH/HCl	q.s. pH 7.4
Purified Water	q.s. 100 mL

- DETD A preferred topical ophthalmic composition useful for treating inflammation and/or tissue oxidative damage:

DETD

Component	% w/v
-----------	-------

Compound E	0.10
<u>Tyloxapol</u>	0.01-0.05
HPMC	0.5
Benzalkonium Chloride	0.01
Sodium Chloride	0.8
Edetate Disodium	0.01
NaOH/HCl	q.s. pH 7.4
Purified Water	q.s. 100 mL

DETD . . . either dry heat or filtered. The sterilized anti-inflammatory agent is weighed aseptically and placed into a pressurized ballmill container. The **tyloxapol**, in sterilized aqueous solution form, is then added to the ballmill container. Sterilized glass balls are then added to the. . .

CLM What is claimed is:

. . . acid; indoprofen; piroprofen; clidanac; fenoprofen; naproxen; fencloxac; meclofenamate; benoxaprofen; carprofen; isofezolac; aceloferac; fenbufen; etodolic acid; fleclozic acid; amfenac; efenamic acid; **bromfenac**; ketoprofen; fenclofenac; alcofenac; orpanoxin; zomopirac; diflunisal; flufenamic acid; niflumic acid; mefenamic acid; pranoprofen; zaltoprofen; indomethacin; sulindac; tolmetin; suprofen; ketorolac; flurbiprofen;. . .

CLM What is claimed is:

. . . acid; indoprofen; piroprofen, clidanac; fenoprofen; naproxen; fencloxac; meclofenamate; benoxaprofen; carprofen; isofezolac; aceloferac; fenbufen; etodolic acid; fleclozic acid; amfenac; efenamic acid; **bromfenac**; ketoprofen; fenclofenac; alcofenac; orpanoxin; zomopirac; diflunisal; flufenamic acid; niflumic acid; mefenamic acid; pranoprofen; zaltoprofen; indomethacin; sulindac; tolmetin; suprofen; ketorolac; flurbiprofen;. . .

CLM What is claimed is:

24. The method according to claim 23, wherein the composition is administered to prevent or alleviate damage to **ophthalmic** tissues.

CLM What is claimed is:

. . . acid; indoprofen; piroprofen; clidanac; fenoprofen; naproxen; fencloxac; meclofenamate; benoxaprofen; carprofen; isofezolac; aceloferac; fenbufen; etodolic acid; fleclozic acid; amfenac; efenamic acid; **bromfenac**; ketoprofen; fenclofenac; alcofenac; orpanoxin; zomopirac; diflunisal; flufenamic acid; niflumic acid; mefenamic acid; pranoprofen; zaltoprofen; indomethacin; sulindac; tolmetin; suprofen; ketorolac; flurbiprofen;. . .

IT Drug delivery systems

(**ophthalmic**; preparation of esters of non-steroidal antiinflammatory agents with antioxidant activity)

L9 ANSWER 33 OF 38 USPATFULL on STN

ACCESSION NUMBER: 97:68150 USPATFULL

TITLE: Preserved **ophthalmic** drug compositions containing polymeric quaternary ammonium compounds

INVENTOR(S): Desai, Suketu Dipakbhai, Fort Worth, TX, United States

PATENT ASSIGNEE(S): Nelms, Diane S., Fort Worth, TX, United States
 Alcon Laboratories, Inc., Fort Worth, TX, United States
 (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5653972		19970805 <--
APPLICATION INFO.:	US 1996-700960		19960821 (8)
RELATED APPLN. INFO.:	Division of Ser. No. US 1994-340763, filed on 16 Nov 1994		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Page, Thurman K.		
ASSISTANT EXAMINER:	Howard, Sharon		
LEGAL REPRESENTATIVE:	Ryan, Patrick M.		
NUMBER OF CLAIMS:	5		
EXEMPLARY CLAIM:	1		
LINE COUNT:	309		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

TI Preserved ophthalmic drug compositions containing polymeric quaternary ammonium compounds

AB Disclosed are storage-stable preserved ophthalmic compositions containing acidic drugs in combination with polymeric quaternary ammonium compounds and boric acid.

SUMM The present invention relates generally to ophthalmic compositions. In particular, the present invention relates to the use of a polymeric quaternary ammonium compound and boric acid to provide preserved, storage-stable ophthalmic compositions of acidic drugs.

SUMM Ophthalmic formulations generally contain one or more active compounds along with excipients such as surfactants, comforting agents, complexing agents, stabilizers, buffering systems, chelating agents, viscosity agents or gelling polymers and anti-oxidants. Ophthalmic formulations which are intended for multidose use require a preservative.

SUMM Organo-mercurials have been used as preservatives in ophthalmic formulations including ophthalmic solutions of acidic drugs. These organo-mercurials include thimerosal, phenylmercuric acetate and phenylmercuric nitrate. Organo-mercurials, however, have limitations due to potential. . .

SUMM Sorbic acid, has also been used to preserve ophthalmic formulations, but it too possesses poor chemical stability as well as poor antimicrobial activity.

SUMM Benzalkonium chloride is a widely used preservative in ophthalmic solutions. However, benzalkonium chloride and other quaternary ammonium compounds are generally considered to be incompatible with ophthalmic compositions of drugs with acidic groups, such as nonsteroidal antiinflammatory drugs ("NSAIDS"). These preservative lose their ability to function as. . .

SUMM U.S. Pat. No. 5,110,493 discloses stable ophthalmic NSAID formulations which do not contain organo-mercurial preservatives. Instead, the reference NSAID formulations use quaternary ammonium compounds, such as cetyltrimethylammonium. . .

- SUMM PCT application WO 94/15597 discloses the use of lauralkonium chloride, the C.sub.12 homolog of benzalkonium chloride, in **ophthalmic** formulations of drugs which are incompatible with benzalkonium chloride. Unlike the mixture of alkyldimethylbenzylammonium chloride known as benzalkonium chloride, this. . . .
- SUMM . . . safe, stable, and able to meet both the United States Pharmacopoeia (USP) and European Pharmacopoeia (Ph.Eur.) preservative effectiveness requirements for **ophthalmic** formulations of acidic drugs has forced pharmaceutical companies to develop more than one formulation of the same drug, with each. . . .
- SUMM U.S. Pat. No. 4,960,799 discloses storage stable aqueous **ophthalmic** compositions containing diclofenac, a nonsteroidal antiinflammatory drug, and/or its pharmaceutically acceptable salts. The reference compositions include EDTA as a stabilizing. . . .
- SUMM . . . None of these references disclose the use of a polymeric quaternary ammonium compound as a preservative in any formulations of **ophthalmic** drugs.
- SUMM . . . discovered that the use of a combination of a polymeric quaternary ammonium compound such as Polyquad® and boric acid in **ophthalmic** compositions of acidic drugs provides a storage-stable composition which has surprisingly good preservative efficacy. This preservative combination of a polymeric quaternary ammonium compound and boric acid is useful in **ophthalmic** compositions of acidic drugs such as prostaglandins, antifungals, antibacterials, and diagnostic agents. This preservative combination is especially useful in **ophthalmic** solutions of drugs containing either a carboxyl group such as non-steroidal antiinflammatory drugs (NSAIDS) or a sulfonamide group such as. . . .
- SUMM Among other factors, the present invention is based on the discovery that **ophthalmic** compositions containing a polymeric quaternary ammonium compound and boric acid may be effectively preserved by the USP and Ph.Eur. preservative. . . .
- SUMM Suitable **ophthalmic** agents which may be included in the compositions of the present invention and administered via the method of the present. . . derivatives; non-steroidal anti-inflammatory agents, including but not limited to those classified as aryl- or heteroaryl-alkanoic acids, such as diclofenac, **bromfenac**, flurbiprofen, suprofen, ketorolac, indomethacin and ketoprofen; anti-bacterials and anti-infectives, including sulfa drugs, such as sulfacetamide sodium, and beta-lactams such as penicillins and cephalosporins; and diagnostic agents such as sodium fluorescein. Combinations of **ophthalmic** agents may also be used in the compositions of the present invention.
- SUMM . . . chlorobutanol, and biguanides such as chlorhexidine and hydroxypropyl methyl biguanide), surfactants (e.g. poloxamers such as Pluronic®; polysorbates such as Tweens®; **tyloxapol**; sarcosinates such as Hamposyl®; and polyethoxylated castor oils such as Cremophor®), and tonicity agents (e.g., sodium chloride, mannitol, dextrose and. . . .
- SUMM The **ophthalmic** compositions of the present invention may additionally contain polymers which will undergo sol-to-gel transition upon exposure to physical or chemical. . . .
- DETD . . . the formulation. The rate or level of antimicrobial activity determined compliance with the USP and/or Ph.Eur. preservative efficacy standards for **ophthalmic** preparations.

DETD The compendial preservative standards for ophthalmic preparations are presented below:

DETD . . . of the preservative challenge study conducted on Formulation A are shown below in Table 1. These results illustrate that an ophthalmic formulation of an acidic drug can be globally preserved, that is, can comply with the USP and Ph.Eur. A preservative effectiveness requirements for ophthalmic preparations, using a combination of a polymeric quaternary ammonium compound and boric acid.

CLM What is claimed is:

1. A method for treating or controlling ocular inflammation comprising the topical ocular application of a preserved storage stable ophthalmic composition comprising a therapeutically-effective amount of one or more acidic non-steroidal anti-inflammatory agents, a combination of an antimicrobial polymeric quaternary . . .

CLM What is claimed is:

5. The method of claim 2 wherein the non-steroidal anti-inflammatory agent is selected from the group consisting of bromfenac and its ophthalmically acceptable salts, esters, amides or prodrugs.

ST ophthalmic prepn quaternary ammonium polymer preservative;
diclofenac borate Polyquad ophthalmic prepn

IT Inflammation inhibitors
(nonsteroidal; preserved ophthalmic drug compns. containing polymeric quaternary ammonium compds.)

IT Biocides

IT Glaucoma (disease)
(preserved ophthalmic drug compns. containing polymeric quaternary ammonium compds.)

IT Diagnosis
(agents, preserved ophthalmic drug compns. containing polymeric quaternary ammonium compds.)

IT Pharmaceutical dosage forms
(ophthalmic, preserved ophthalmic drug compns. containing polymeric quaternary ammonium compds.)

IT Quaternary ammonium compounds, biological studies
(polymers, preserved ophthalmic drug compns. containing polymeric quaternary ammonium compds.)

IT 53-86-1, Indomethacin 5104-49-4, Flurbiprofen 10043-35-3, Boric acid, biological studies 10043-35-3D, Boric acid, polyol complexes 15307-79-6, Sodium diclofenac 15307-86-5, Diclofenac 22071-15-4, Ketoprofen 40828-46-4, Suprofen 74103-06-3, Ketorolac 75345-27-6, Polyquaternium-1 91714-94-2, Bromfenac
(preserved ophthalmic drug compns. containing polymeric quaternary ammonium compds.)

L9 ANSWER 34 OF 38 USPATFULL on STN

ACCESSION NUMBER: 97:14409 USPATFULL

TITLE: Preserved ophthalmic drug compositions
containing polymeric quaternary ammonium compounds

INVENTOR(S): Desai, Suketu D., Fort Worth, TX, United States
Nelms, Diane S., Fort Worth, TX, United States

PATENT ASSIGNEE(S): Alcon Laboratories, Inc., Fort Worth, TX, United States
(U.S. corporation)

	NUMBER	KIND	DATE	
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PATENT INFORMATION:	US 5603929		19970218	<--
APPLICATION INFO.:	US 1994-340763		19941116	(8)
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Page, Thurman K.			
ASSISTANT EXAMINER:	Howard, Sharon			
LEGAL REPRESENTATIVE:	Ryan, Patrick M.			
NUMBER OF CLAIMS:	20			
EXEMPLARY CLAIM:	1			
LINE COUNT:	361			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

TI Preserved ophthalmic drug compositions containing polymeric quaternary ammonium compounds

AB Disclosed are storage-stable preserved ophthalmic compositions containing acidic drugs in combination with polymeric quaternary ammonium compounds and boric acid.

SUMM The present invention relates generally to ophthalmic compositions. In particular, the present invention relates to the use of a polymeric quaternary ammonium compound and boric acid to provide preserved, storage-stable ophthalmic compositions of acidic drugs.

SUMM Ophthalmic formulations generally contain one or more active compounds along with excipients such as surfactants, comforting agents, complexing agents, stabilizers, buffering systems, chelating agents, viscosity agents or gelling polymers and anti-oxidants. Ophthalmic formulations which are intended for multidose use require a preservative.

SUMM Organo-mercurials have been used as preservatives in ophthalmic formulations including ophthalmic solutions of acidic drugs. These organo-mercurials include thimerosal, phenylmercuric acetate and phenylmercuric nitrate. Organo-mercurials, however, have limitations due to potential. . .

SUMM Sorbic acid, has also been used to preserve ophthalmic formulations, but it too possesses poor chemical stability as well as poor antimicrobial activity.

SUMM Benzalkonium chloride is a widely used preservative in ophthalmic solutions. However, benzalkonium chloride and other quaternary ammonium compounds are generally considered to be incompatible with ophthalmic compositions of drugs with acidic groups, such as nonsteroidal antiinflammatory drugs ("NSAIDS"). These preservative lose their ability to function as. . .

SUMM U.S. Pat. No. 5,110,493 discloses stable ophthalmic NSAID formulations which do not contain organo-mercurial preservatives. Instead, the reference NSAID formulations use quaternary ammonium compounds, such as cetyltrimethylammonium. . .

SUMM PCT application WO 94/15597 discloses the use of lauralkonium chloride, the C.sub.12 homolog of benzalkonium chloride, in ophthalmic formulations of drugs which are incompatible with benzalkonium chloride. Unlike the mixture of alkyldimethylbenzylammonium chloride known as benzalkonium chloride, this. . .

SUMM . . . stable, and able to meet both the United States Pharmacopoeia (USP) and European Pharmacopoeia (Ph. Eur.) preservative effectiveness requirements for ophthalmic formulations of acidic drugs has forced pharmaceutical companies to develop more than one formulation of the same drug, with each. . . .

SUMM U.S. Pat. No. 4,960,799 discloses storage stable aqueous ophthalmic compositions containing diclofenac, a nonsteroidal antiinflammatory drug, and/or its pharmaceutically acceptable salts. The reference compositions include EDTA as a stabilizing. . . .

SUMM . . . contact lens and artificial tear solutions, also discloses the use of certain polymeric quaternary ammonium compounds in formulations containing certain ophthalmic drugs. However, neither this reference nor any of the other references mentioned above discloses the use of a polymeric quaternary ammonium compound as a preservative in formulations of acidic ophthalmic drugs, that is, drugs which may be incompatible with positively charged preservatives.

SUMM . . . discovered that the use of a combination of a polymeric quaternary ammonium compound such as POLYQUAD® and boric acid in ophthalmic compositions of acidic drugs provides a storage-stable composition which has surprisingly good preservative efficacy. This preservative combination of a polymeric quaternary ammonium compound and boric acid is useful in ophthalmic compositions of acidic drugs such as prostaglandins, antifungals, antibacterials, and diagnostic agents. This preservative combination is especially useful in ophthalmic solutions of drugs containing either a carboxyl group such as non-steroidal anti-inflammatory drugs (NSAIDS) or a sulfonamide group such as. . . .

SUMM Among other factors, the present invention is based on the discovery that ophthalmic compositions containing a polymeric quaternary ammonium compound and boric acid may be effectively preserved by the USP and Ph. Eur. . . .

DETD Suitable ophthalmic agents which may be included in the compositions of the present invention and administered via the method of the present. . . . derivatives; non-steroidal anti-inflammatory agents, including but not limited to those classified as aryl- or heteroaryl-alkanoic acids, such as diclofenac, bromfenac, flurbiprofen, suprofen, ketorolac, indomethacin and ketoprofen; anti-bacterials and anti-infectives, including sulfa drugs, such as sulfacetamide sodium, and beta-lactams such as penicillins and cephalosporins; and diagnostic agents such as sodium fluorescein. Combinations of ophthalmic agents may also be used in the compositions of the present invention.

DETD . . . chlorobutanol, and biguanides such as chlorhexidine and hydroxypropyl methyl biguanide), surfactants (e.g. poloxamers such as Pluronic®; polysorbates such as Tweens®; tyloxapol; sarcosinates such as Hamposyl®; and polyethoxylated castor oils such as Cremophor®), and tonicity agents (e.g., sodium chloride, mannitol, dextrose and. . . .

DETD The ophthalmic compositions of the present invention may additionally contain polymers which will undergo sol-to-gel transition upon exposure to physical or chemical. . . .

DETD . . . formulation. The rate or level of antimicrobial activity determined compliance with the USP and/or Ph. Eur. preservative efficacy standards for ophthalmic preparations.

DETD The compendial preservative standards for ophthalmic

preparations are presented below:

DETD . . . of the preservative challenge study conducted on Formulation A are shown below in Table 1. These results illustrate that an ophthalmic formulation of an acidic drug can be globally preserved, that is, can comply with the USP and Ph. Eur. A preservative effectiveness requirements for ophthalmic preparations, using a combination of a polymeric quaternary ammonium compound and boric acid.

CLM What is claimed is:

1. A storage stable ophthalmic composition comprising a therapeutically effective amount of one or more acidic ophthalmic agents, a combination of an antimicrobial polymeric quaternary ammonium compound and boric acid in an amount effective to meet at . . . minimum United States Pharmacopeia XXII and European Pharmacopeia (1994) preservative effectiveness requirements, and an ophthalmically acceptable vehicle; wherein the acidic ophthalmic agent is selected from the group consisting of anti-glaucoma and non-steroidal anti-inflammatory agents; provided that the composition does not contain. . .

CLM What is claimed is:

2. The composition of claim 1 wherein the ophthalmic agent is a non-steroidal anti-inflammatory agent.

CLM What is claimed is:

. . . The composition of claim 3 wherein the non-steroidal anti-inflammatory agent is selected from the group consisting of: diclofenac, flurbiprofen, suprofen, bromfenac, keterolac, indomethacin, ketaprofen, and ophthalmically acceptable salts, esters, amides or prodrugs thereof.

CLM What is claimed is:

7. The composition of claim 4 wherein the non-steroidal anti-inflammatory agent is selected from the group consisting of bromfenac and its ophthalmically acceptable salts, esters, amides, or prodrugs thereof.

CLM What is claimed is:

19. An ophthalmic formulation comprising diclofenac or an ophthalmically acceptable salt, ester, amide or prodrug thereof, and a combination of an antimicrobial polymeric. . .

ST ophthalmic prepn quaternary ammonium polymer preservative;
diclofenac borate Polyquad ophthalmic prepn

IT Inflammation inhibitors

(nonsteroidal; preserved ophthalmic drug compns. containing polymeric quaternary ammonium compds.)

IT Biocides

IT Glaucoma (disease)

(preserved ophthalmic drug compns. containing polymeric quaternary ammonium compds.)

IT Diagnosis

(agents, preserved ophthalmic drug compns. containing polymeric quaternary ammonium compds.)

IT Pharmaceutical dosage forms

(ophthalmic, preserved ophthalmic drug compns.)

containing polymeric quaternary ammonium compds.)

IT Quaternary ammonium compounds, biological studies
(polymers, preserved ophthalmic drug compns. containing polymeric quaternary ammonium compds.)

IT 53-86-1, Indomethacin 5104-49-4, Flurbiprofen 10043-35-3, Boric acid, biological studies 10043-35-3D, Boric acid, polyol complexes 15307-79-6, Sodium diclofenac 15307-86-5, Diclofenac 22071-15-4, Ketoprofen 40828-46-4, Suprofen 74103-06-3, Ketorolac 75345-27-6, Polyquaternium-1 91714-94-2, Bromfenac
(preserved ophthalmic drug compns. containing polymeric quaternary ammonium compds.)

L9 ANSWER 35 OF 38 USPAT2 on STN

ACCESSION NUMBER: 2004:334304 USPAT2

TITLE: Cyclooxygenase-2 inhibitor compositions having rapid onset of therapeutic effect

INVENTOR(S): Kararli, Tugrul T., Skokie, IL, UNITED STATES
Kontny, Mark J., Libertyville, IL, UNITED STATES
Desai, Subhash, Wilmette, IL, UNITED STATES
Hageman, Michael J., Portage, MI, UNITED STATES
Haskell, Royal J., Kalamazoo, MI, UNITED STATES(4)
PATENT ASSIGNEE(S): Pharmacia Corporation, St. Louis, MO, UNITED STATES
(U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 7172769	B2	20070206	
	WO 2001041760		20010614	<--
APPLICATION INFO.:	US 2000-31898		20001206	(10)
	WO 2000-US32434		20001206	
			20020730	PCT 371 date

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-169856P	19991209 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Azpuru, Carlos A.	
LEGAL REPRESENTATIVE:	Fitzsimmons, Patricia K., Ashbrook, Charles	
NUMBER OF CLAIMS:	17	
EXEMPLARY CLAIM:	1,2	
NUMBER OF DRAWINGS:	4 Drawing Figure(s); 3 Drawing Page(s)	
LINE COUNT:	1893	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . conditions such as psoriasis, eczema, acne, burns, dermatitis and ultraviolet radiation damage including sunburn, and post-operative inflammation including that following ophthalmic surgery such as cataract surgery or refractive surgery.

DETD Such compositions are useful in treatment of ophthalmic diseases, such as retinitis, conjunctivitis, retinopathies, uveitis, ocular photophobia, and of acute injury to the eye tissue.

DETD . . . ammonium salicylate, ampiroxicam, amtolmetin guacil, anileridine, antipyrine, antipyrine salicylate, antrafenine, apazone,

bendazac, benorylate, benoxaprofen, benzpiperylon, benzydamine, benzylmorphine, bermoprofen, bezitrarnide, α -bisabolol, **bromfenac**, p-bromoacetanilide, 5-bromosalicylic acid acetate, bromosaligenin, bucin, bucloxic acid, bucolome, bufexamac, bumadizon, buprenorphine, butacetin, butibufen, butophanol, calcium acetylsalicylate, carbamazepine, carbiphen, carprofen, . . .

DETD . . . In this embodiment the surface modifying agent is a nonionic liquid polymer of the alkylaryl polyether alcohol type, for example **tyloxapol**. Optionally an additional surface modifying agent can be present.

DETD . . . of an oil, a selective COX-2 inhibitory drug in the presence of surface modifying agents (e.g., gelatin, casein, lecithin, polyvinylpyrrolidone, **tyloxapol**, poloxamers, other block polymers, etc.) substantially as disclosed in above-cited U.S. Pat. No. 5,560,931. In this embodiment, the drug particles. . .

DETD . . . comprising a first particle distribution of a selective COX-2 inhibitory drug together with a surface modifying agent such as polysulfated **tyloxapol** by a process comprising the steps of (a) placing the dispersion between a first electrode and a second electrode; and. . .

DETD . . . fatty acid esters, for example glyceryl monostearate, sorbitan esters, for example sorbitan monolaurate, sorbitan monooleate, sorbitan monopalmitate and sorbitan monostearate, **tyloxapol**, and mixtures thereof. Such wetting agents, if present, constitute in total about 0.25% to about 15%, preferably about 0.4% to. . .

L9 ANSWER 36 OF 38 USPAT2 on STN

ACCESSION NUMBER: 2004:307964 USPAT2

TITLE: Dual-release compositions of a cyclooxygenase-2 inhibitor

INVENTOR(S): Desai, Subhash, Wilmette, IL, UNITED STATES
Nadkarni, Sreekant R., Gurnee, IL, UNITED STATES
Wald, Randy J., Portage, MI, UNITED STATES
DeBrincat, Gary A., Battle Creek, MI, UNITED STATES

PATENT ASSIGNEE(S): Pharmacia Corporation (of Pfizer, Inc.), St Louis, MO, UNITED STATES (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 7220434	B2	20070522	
	WO 2001045706		20010628	<--
APPLICATION INFO.:	US 2000-169039		20001220	(10)
	WO 2000-US34754		20001220	
			20040223	PCT 371 date
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	GRANTED			
PRIMARY EXAMINER:	Hartley, Michael G.			
ASSISTANT EXAMINER:	Ebrahim, Nabila			
LEGAL REPRESENTATIVE:	Fitzsimmons, Patricia K., Ashbrook, Charles W.			
NUMBER OF CLAIMS:	18			
EXEMPLARY CLAIM:	1			
NUMBER OF DRAWINGS:	1 Drawing Figure(s); 1 Drawing Page(s)			
LINE COUNT:	2151			
CAS INDEXING IS AVAILABLE FOR THIS PATENT.				

DETD . . . conditions such as psoriasis, eczema, acne, burns, dermatitis and ultraviolet radiation damage including sunburn, and post-operative inflammation including that following ophthalmic surgery such as cataract surgery or refractive surgery.

DETD Such compositions are useful in treatment of ophthalmic diseases, such as retinitis, conjunctivitis, retinopathies, uveitis, ocular photophobia, and of acute injury to the eye tissue.

DETD . . . ammonium salicylate, ampiroxicam, amtolmetin guacil, anileridine, antipyrine, antipyrine salicylate, antrafenine, apazone, bendazac, benorylate, benoxaprofen, benzpiperylon, benzydamine, benzylmorphine, bermoprofen, bezitramide, α -bisabolol, **bromfenac**, p-bromoacetanilide, 5-bromosalicylic acid acetate, bromosaligenin, bucetin, bucloxic acid, bucolome, bufexamac, bumadizon, buprenorphine, butacetin, butibufen, butophanol, calcium acetylsalicylate, carbamazepine, carbiphen, carprofen, . . .

DETD . . . fatty acid esters, for example glyceryl monostearate, sorbitan esters, for example sorbitan monolaurate, sorbitan monooleate, sorbitan monopalmitate and sorbitan monostearate, tyloxapol, and mixtures thereof. Such wetting agents, if present, constitute in total about 0.25% to about 15%, preferably about 0.4% to. . .

L9 ANSWER 37 OF 38 USPAT2 on STN

ACCESSION NUMBER: 2002:48624 USPAT2

TITLE: Compositions and methods for treating ophthalmic and otic infections

INVENTOR(S): Cagle, Gerald, Fort Worth, TX, United States
 Abshire, Robert L., Fort Worth, TX, United States
 Stroman, David W., Irving, TX, United States
 McLean, Celeste H., Fort Worth, TX, United States
 Clark, Linda L., Grandview, TX, United States
 Yanni, John M., Burleson, TX, United States

PATENT ASSIGNEE(S): Alcon Manufacturing, Ltd., Fort Worth, TX, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6440964	B2	20020827	<--
APPLICATION INFO.:	US 2001-887771		20010622	(9)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 577262			

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-102504P	19980930 (60)
	US 1998-102506P	19980930 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Fay, Zohreh	
LEGAL REPRESENTATIVE:	Brown, Gregg C.	
NUMBER OF CLAIMS:	6	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	1 Drawing Figure(s); 1 Drawing Page(s)	
LINE COUNT:	510	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		

- TI Compositions and methods for treating ophthalmic and otic infections
- AB Ophthalmic, otic and nasal compositions containing a new class of antibiotics (e.g., moxifloxacin) are disclosed. The compositions preferably also contain one or more anti-inflammatory agents. The compositions may be utilized to treat ophthalmic, otic and nasal conditions by topically applying the compositions to the affected tissues. The compositions and methods of the invention are particularly useful in the treatment of acute otitis externa infections and ophthalmic infections attributable to one or both of two newly identified Microbacterium species, Microbacterium otitidis and Microbacteriumalconae.
- SUMM The present invention is directed to the provision of topical antibiotic pharmaceutical compositions for the treatment of ophthalmic, otic and nasal infections, particularly bacterial infections, and to methods of treating ophthalmic, otic and nasal infections by applying those compositions to the affected tissues. The compositions and methods of the invention are. . .
- SUMM Quinolone antibiotics have been previously utilized to treat ophthalmic and otic infections. For example, a topical ophthalmic composition containing the quinolone ciprofloxacin is marketed by Alcon Laboratories, Inc. under the name CILOXAN.TM. (Ciprofloxacin 0.3%) Ophthalmic Solution, and a topical otic composition containing a combination of ciprofloxacin and hydrocortisone is marketed by Alcon Laboratories, Inc. under the name CIPRO.TM. HC. The following quinolones have also been utilized in ophthalmic antibiotic compositions:
- SUMM The foregoing quinolone antibiotic compositions are generally effective in treating ophthalmic infections, and have distinct advantages over prior ophthalmic antibiotic compositions, particularly those having relatively limited spectrums of antimicrobial activity, such as: neomycin, polymyxin B, gentamicin and tobramycin, which. . . and bacitracin, gramicidin, and erythromycin, which are primarily active against gram positive pathogens. However, despite the general efficacy of the ophthalmic quinolone therapies currently available, there is a need for improved compositions and methods of treatment based on the use of antibiotics that are more effective than existing antibiotics against key ophthalmic pathogens, and less prone to the development of resistance by those pathogens.
- SUMM Ophthalmic, otic and nasal infections are frequently accompanied by inflammation of the infected ophthalmic, otic and nasal tissues and perhaps even surrounding tissues. Similarly, ophthalmic, otic and nasal surgical procedures that create a risk of microbial infections frequently also cause inflammation of the affected tissues. Thus, there is also a need for ophthalmic, otic and nasal pharmaceutical compositions that combine the anti-infective activity of one or more antibiotics with the anti-inflammatory activity of. . .
- SUMM The invention is based on the use of a potent new class of antibiotics to treat ophthalmic, otic and nasal infections, as well as the use of these antibiotics prior to surgery to sterilize the surgical field and prophylactically following surgery or other trauma to

ophthalmic, otic or nasal tissues to minimize the risk of infection. The compositions of the present invention may also be administered to the affected tissues during ophthalmic, otic or nasal surgical procedures to prevent or alleviate post-surgical infection. As utilized herein, the terms "treat", "treating" and derivations. . . .

SUMM The compositions preferably also contain one or more anti-inflammatory agents to treat inflammation associated with infections of ophthalmic, otic or nasal tissues. The anti-inflammatory component of the compositions is also useful in treating inflammation associated with physical trauma to ophthalmic, otic or nasal tissues, including inflammation resulting from surgical procedures. The compositions of the present invention are therefore particularly useful in treating inflammation associated with trauma to ophthalmic, otic or nasal tissues wherein there is either an infection or a risk of an infection resulting from the trauma.

SUMM Examples of ophthalmic conditions that may be treated with the compositions of the present invention include conjunctivitis, keratitis, blepharitis, dacryocystitis, hordeolum and corneal ulcers. The compositions of the invention may also be used prophylactically in connection with various ophthalmic surgical procedures that create a risk of infection.

SUMM . . . that have been identified as being associated with acute otitis externa infections have also been discovered to be associated with ophthalmic infections. As indicated above, the antibiotics utilized in the present invention have a high level of antimicrobial activity against these newly discovered ophthalmic pathogens, and as a result, the compositions of the present invention are particularly useful in treating ophthalmic infections involving these species.

SUMM The compositions of the present invention are specially formulated for topical application to ophthalmic, otic and nasal tissues. The compositions are preferably sterile, and have physical properties (e.g., osmolality and pH) that are specially suited for application to ophthalmic, otic and nasal tissues, including tissues that have been compromised as the result of preexisting disease, trauma, surgery or other. . . .

DETD . . . to as the "minimum bactericidal concentration" or "MBC". The minimum inhibitory concentration of Moxifloxacin for several bacteria commonly associated with ophthalmic, otic and nasal infections are provided in the following table:

DETD Microbacterium otitidis and Microbacterium alconae have also been discovered to be pathogens in infections of ophthalmic tissues, such as conjunctivitis and blepharitis. The compositions of the present invention are therefore particularly useful in treating ophthalmic infections involving one or both of these species.

DETD The appropriate antibiotic concentration for ophthalmic compositions will generally be an amount of one or more antibiotics of formula (I) sufficient to provide a concentration in. . . . to or greater than the MIC.sub.90 level for the selected antibiotic(s), relative to gram-negative and gram-positive organisms commonly associated with ophthalmic infections. The appropriate concentration for otic and nasal compositions will generally be an amount of one or more antibiotics of. . . .

- DETD The preferred glucocorticoids for ophthalmic and otic use include dexamethasone, loteprednol, rimexolone, prednisolone, fluorometholone, and hydrocortisone. The preferred glucocorticoids for nasal use include mometasone, fluticasone,
- DETD described in U.S. Pat. No. 5,223,493 (Boltralik) are also preferred steroidal anti-inflammatory agents, particularly with respect to compositions for treating ophthalmic inflammation. The following compounds are especially preferred: ##STR4##
- DETD to as cyclooxygenase type I and type II inhibitors, such as diclofenac, flurbiprofen, ketorolac, suprofen, nepafenac, amfenac, indomethacin, naproxen, ibuprofen, bromfenac, ketoprofen, meclofenamate, piroxicam, sulindac, mefanamic acid, diflusal, oxaprozin, tolmetin, fenoprofen, benoxaprofen, nabumetone, etodolac, phenylbutazone, aspirin, oxyphenbutazone, NCX-4016, HCT-1026, NCX-284, NCX-456,
- DETD agents selected and the type of inflammation being treated. The concentrations will be sufficient to reduce inflammation in the targeted ophthalmic, otic or nasal tissues following topical application of the compositions to those tissues. Such an amount is referred to herein. . . .
- DETD The compositions are typically administered to the affected ophthalmic, otic or nasal tissues by topically applying one to four drops of a sterile solution or suspension, or a comparable. . . . four times per day. However, the compositions may also be formulated as irrigating solutions that are applied to the affected ophthalmic, otic or nasal tissues during surgical procedures.
- DETD The ophthalmic, otic and nasal compositions of the present invention will contain one or more compounds of formula (I) and preferably one. . . . agents, in pharmaceutically acceptable vehicles. The compositions will typically have a pH in the range of 4.5 to 8.0. The ophthalmic compositions must also be formulated to have osmotic values that are compatible with the aqueous humor of the eye and ophthalmic tissues. Such osmotic values will generally be in the range of from about 200 to about 400 milliosmoles per kilogram. . . .
- DETD Ophthalmic, otic and nasal pharmaceutical products are typically packaged in multidose form. Preservatives are thus required to prevent microbial contamination during. . . .
- DETD The following examples are provided to further illustrate the ophthalmic, otic and nasal compositions of the present invention.
- DETD

Ophthalmic/Otic/Nasal Solution

Ingredient Amount (wt. %)

Moxifloxacin 0.35

Sodium Acetate 0.03

Acetic Acid 0.04

Mannitol 4.60

EDTA 0.05

Benzalkonium Chloride. . . .

DETD

Ophthalmic/Otic/Nasal Suspension

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Ingredient Amount (wt. %)

Moxifloxacin 0.3
Dexamethasone, Micronized USP 0.10
Benzalkonium Chloride 0.01
Edetate Disodium, USP 0.01
Sodium Chloride, USP 0.3
Sodium Sulfate, USP 1.2
Tyloxapol, USP 0.05
Hydroxyethylcellulose 0.25
Sulfuric Acid and/or q.s. for pH adjustment to 5.5
Sodium Hydroxide, NF
Purified Water, USP q.s. to 100
DETD

Ophthalmic Ointment

Ingredient Amount (wt. %)

Moxifloxacin 0.35
Mineral Oil, USP 2.0
White petrolatum, USP q.s 100
DETD

Ophthalmic Ointment

Ingredient Amount (wt. %)

Moxifloxacin 0.3
Fluorometholone Acetate, USP 0.1
Chlorobutanol, Anhydrous, NF 0.5
Mineral Oil, USP 5

. . .
CLM What is claimed is:
1. A topical pharmaceutical composition for treating acute otitis externa infections or ophthalmic infections attributable to a Microbacterium species selected from the group consisting of Microbacterium otitidis and Microbacterium alconae, comprising of one.

. . .
CLM What is claimed is:
6. A method of treating acute otitis externa infections or ophthalmic infections attributable to a Microbacterium species selected from the group consisting of Microbacterium otitidis and Microbacterium alconae, which comprises instilling. . .

IT Drug delivery systems
(ophthalmic; antibiotic compns. for treatment of eye and ear and nose disorders)

L9 ANSWER 38 OF 38 USPAT2 on STN

ACCESSION NUMBER: 2002:48047 USPAT2

TITLE: Use of a celecoxib composition for fast pain relief

INVENTOR(S): Karim, Aziz, Skokie, IL, United States

Brugger, Andrew M., Libertyville, IL, United States

Gao, Ping, Portage, MI, United States

Hassan, Fred, Peapack, NJ, United States

Forbes, James C., Glenview, IL, United States

Jagoe

10/525006

PATENT ASSIGNEE(S): Pharmacia Corporation, St. Louis, MO, United States
(U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6579895	B2	20030617	<--
APPLICATION INFO.:	US 2001-866165		20010525	(9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-207729P	20000526 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Cook, Rebecca	
LEGAL REPRESENTATIVE:	Harness, Dickey & Pierce	
NUMBER OF CLAIMS:	29	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	4 Drawing Figure(s); 4 Drawing Page(s)	
LINE COUNT:	1140	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . of ICI), propylene glycol laurate (e.g., Lauroglycol.TM. of Gattefosse), sodium lauryl sulfate, sorbitan monolaurate, sorbitan monooleate, sorbitan monopalmitate, sorbitan monostearate, **tyloxapol**, and mixtures thereof. Presently preferred examples include polysorbate 80 and sodium lauryl sulfate.

DETD . . . conditions such as psoriasis, eczema, acne, burns, dermatitis and ultraviolet radiation damage including sunburn, and post-operative inflammation including that following **ophthalmic** surgery such as cataract surgery or refractive surgery.

DETD Such compositions are useful in treatment of **ophthalmic** diseases, such as retinitis, conjunctivitis, retinopathies, uveitis, ocular photophobia, and of acute injury to the eye tissue.

DETD . . . ammonium salicylate, ampiroxicam, amtolmetin guacil, anileridine, antipyrine, antipyrine salicylate, antrafenine, apazone, bendazac, benorylate, benoxaprofen, benzpiperylon, benzydamine, benzylmorphine, bermoprofen, bezitramide, α -bisabolol, **bromfenac**, p-bromoacetanilide, 5-bromosalicylic acid acetate, bromosaligenin, bucetin, bucloxic acid, bucolome, bufexamac, bumadizon, buprenorphine, butacetin, butibufen, butophanol, calcium acetylsalicylate, carbamazepine, carbiphen, carprofen, . . .

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